West Nile Virus Disease

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To identify areas in which West Nile virus (WNV) is being transmitted.
2. To target areas for public education about reducing mosquito habitats and preventing mosquito bites.
3. To provide information for mosquito control and environmental health initiatives.

B. Legal Reporting Requirements

1. Health care providers: notifiable to local health jurisdiction within 3 work days.
2. Hospitals: notifiable to local health jurisdiction within 3 work days.
3. Laboratories: isolation of WNV, or detection of virus specific antibody or viral nucleic acid notifiable to local health jurisdiction of the patient's residence within 2 work days.
4. Local health jurisdictions: notifiable to Washington State Department of Health Communicable Disease Epidemiology Section (DOH CDES) within 7 days of case investigation completion or summary information required within 21 days.
5. Veterinarians: notifiable to the local health jurisdiction or to Washington State Department of Agriculture.

C. Local Health Jurisdiction Investigation Responsibilities

1. When possible, alert the DOH CDES about possible cases. Identify unusual exposures and potential sources of transmission (i.e., donor or recipient of blood products, tissue or organs) within 24 hours of the initial report.
2. Facilitate transport of specimens (e.g., serum or CSF) to the Washington State Department of Health Public Health Laboratories (DOH PHL) if initial testing or confirmatory testing is needed. Please call DOH CDES prior to submitting specimens (206-418-5500).
3. Report all *confirmed* and *probable* cases to DOH CDES (see definitions below). Complete the West Nile virus case report form (http://www.doh.wa.gov/notify/forms/wnv.pdf) and enter the data into the Public Health Issues Management System (PHIMS) as "West Nile Virus Disease" (*Note:* not "Arboviral Disease").
4. Fill out the Centers for Disease Control and Prevention WNV enhanced surveillance form found at: http://www.doh.wa.gov/notify/forms/wnv-suppform.doc and fax to CDES (206) 418-5515.

2. THE DISEASE AND ITS EPIDEMIOLOGY

Background

West Nile virus (WNV) was first isolated in 1937 from a febrile woman in the West Nile

District of Uganda. WNV was recognized as a cause of severe human meningoencephalitis in elderly patients during an outbreak in Israel in 1957. It was first reported in North America in 1999 during an outbreak in New York City, and since then has spread east to west across the United States.

A. Etiologic Agent

West Nile virus is a single-stranded RNA virus of the family *Flaviviridae*, genus *Flavivirus*. It is a member of the Japanese encephalitis virus serocomplex, which contains several medically important viruses associated with human encephalitis: Japanese encephalitis, St. Louis encephalitis, Murray Valley encephalitis, and Kunjin virus (an Australian subtype of West Nile virus). The close antigenic relationship of the flaviviruses, particularly those belonging to the Japanese encephalitis complex, accounts for the serologic cross-reactions observed in the diagnostic laboratory.

B. Description of Illness

Serosurveys indicate that about 80% of those infected with WNV are asymptomatic. Approximately 20% of infected individuals present with **WNV non-neuroinvasive disease** (also known as WNV Fever) and <1% of infected individuals present with **WNV neuroinvasive disease**. WNV non-neuroinvasive disease is a febrile illness of sudden onset, often accompanied by headache, myalgias, malaise, and gastrointestinal symptoms. Rash and lymphadenopathy occasionally occur. Symptoms generally last 3 to 6 days but may last for weeks. WNV neuroinvasive disease primarily presents as meningitis or encephalitis, but can present with other rare neurologic manifestations such acute flaccid paralysis, cranial nerve abnormalities, and optic neuritis. The incidence and case fatality rate of WNV neuroinvasive disease increase with age, with the greatest risk occurring in persons > 50 years old. Among those with severe illness due to West Nile virus, case-fatality rates range from 3% to 15% and are highest among the elderly.

C. West Nile Virus Infections in Washington State

Washington State conducts surveillance for WNV infections in humans, birds, mosquitoes, horses and other animals. The first detections of the virus in Washington occurred in 2002; the first locally acquired human infections were reported in 2006 from Pierce and Clark counties. For current or historical information about WNV in Washington, visit: http://www.doh.wa.gov/ehp/ts/Zoo/WNV/WNV.html

D. Vectors and Reservoirs

West Nile virus is maintained in an enzootic cycle involving vector mosquitoes and many bird reservoir species. Although corvids (crows, ravens, magpies, jays) infected with WNV often become ill and die, most infected birds survive and do not have any symptoms. Competent bird reservoirs may have virus circulating in their bloodstream for 1 to 4 days after contracting WNV, and mosquitoes that feed on them during that period can become infected. WNV is transmitted mainly by mosquitoes in the *Culex* subgenus, though many other mosquito species are also known to become infected. More than 300 native and exotic bird species have been diagnosed with WNV infection in the United States. People, horses, and most other mammals do not develop infectious-level viremias, and are considered to be "dead-end" or incidental hosts.

E. Modes of Transmission

The main route of transmission for West Nile virus is through the bite of an infected mosquito. In very rare cases, WNV also has been transmitted through blood transfusions, tissue/organ transplants, laboratory percutaneous injuries, transplacentally, and possibly via breast milk.

F. Incubation Period

Usually 2 to 14 days.

G. Period of Communicability

People may develop a short lived (2–3 day) low-level viremia that can contaminate blood units; blood collection centers screen donated units to prevent this from occurring. Transmission through organ transplantation, transplacentally, and via breast milk are very rare. WNV is not spread through casual contact such as touching or kissing a person with the virus.

H. Treatment

Treatment is supportive. Treatment for severe neuroinvasive infections often involves hospitalization, intravenous fluids, respiratory support, and prevention of secondary infections.

Controlled trials investigating specific treatments are ongoing.

3. CASE DEFINITION

A. Clinical Criteria for Diagnosis

WNV infections are classified as either neuroinvasive or non-neuroinvasive, according to the following criteria:

Neuroinvasive disease requires the presence of fever and at least one of the following, as documented by a physician and in the absence of a more likely clinical explanation:

- Acutely altered mental status (e.g., disorientation, obtundation, stupor, or coma), or
- Other acute signs of central or peripheral neurologic dysfunction (e.g., paresis or paralysis, nerve palsies, sensory deficits, abnormal reflexes, generalized convulsions, or abnormal movements), or
- Pleocytosis (increased white blood cell concentration in cerebrospinal fluid [CSF]) associated with illness clinically compatible with meningitis (e.g., headache or stiff neck).

Non-neuroinvasive disease requires, at minimum, all of the following:

- Presence of documented fever, as measured by the patient or clinician, and
- Absence of neuroinvasive disease (as described above), and
- Absence of a more likely clinical explanation.

B. Laboratory Criteria for Diagnosis

1. Virus-specific immunoglobulin M (IgM) antibodies demonstrated in CSF by antibody-capture enzyme immunoassay (EIA), or
2. Virus-specific IgM antibodies demonstrated in serum by antibody-capture EIA and confirmed by demonstration of virus-specific serum immunoglobulin G (IgG) antibodies in the same or a later specimen by another serologic method (e.g., plaque reduction neutralization or hemagglutination inhibition) or,
3. Fourfold or greater change in serum antibody titer, or
4. Isolation of virus from, or demonstration of viral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid.

   Note: See "Specimen Collection" section for appropriate timing for specimen collection.

C. Case Definition

Probable: a clinically compatible case occurring during a period when arboviral transmission is likely with the following supportive serology: 1) serum IgM antibodies detected by antibody-capture EIA without a confirmatory test for virus-specific serum IgG antibodies in the same or a later specimen, or 2) a single or stable elevated titer (≤ two-fold change) of virus-specific serum antibodies;

Confirmed: a clinically compatible case that is laboratory confirmed.

4. DIAGNOSIS AND LABORATORY SERVICES

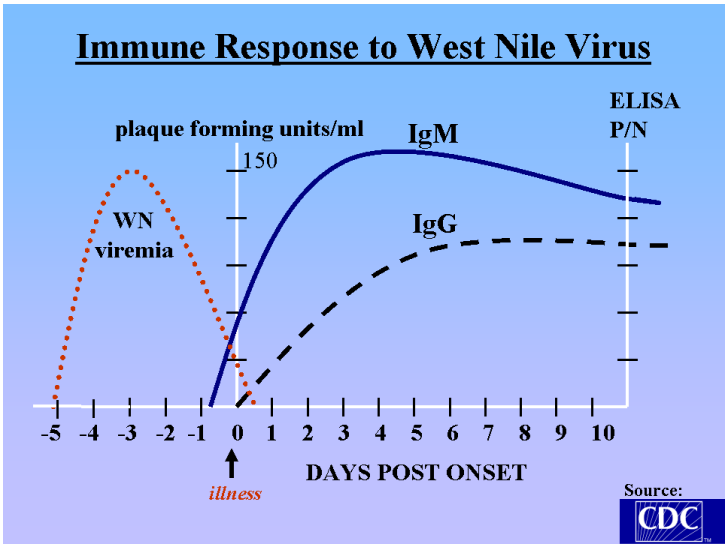
A. Diagnosis

The most efficient diagnostic method is detection of IgM antibody to WNV in serum collected within eight to 14 days of illness onset *or* CSF collected within 8 days of illness onset using the IgM antibody-capture enzyme immunoassay (MAC-EIA) or microsphere immunoassay (MIA). More than 90% of those infected have detectible serum IgM eight days after onset. The EIA can exhibit serologic cross-reactivity in patients who have been recently vaccinated against or recently infected with closely related flaviviruses (e.g., yellow fever, Japanese encephalitis, dengue). In addition, since most WNV infections are asymptomatic and IgM can persist for 6 months or longer, the presence of IgM in residents from an endemic area may indicate a previous rather than current infection. The diagnosis can also be confirmed by demonstrating a four-fold rise in antibody titer between acute and convalescent (2–3 weeks after acute) serum specimens.

The plaque-reduction neutralization test (PRNT) is the most specific test for the arthropod-borne flaviviruses and can be used to help distinguish false-positive results from an IgM antibody-capture enzyme-linked immunosorbent assay. The PRNT must be preformed under biosafety level 3 conditions.

Reverse transcription polymerase chain reaction (RT-PCR) assay to detect WNV nucleic acid in blood or CSF is useful for evaluation of patients with immune dysfunction, but is not recommended for routine diagnosis of WNV disease.

Other antibody detecting diagnostic assays, such as hemagglutination inhibition and indirect fluorescent antibody tests, may be available at commercial laboratories.



B. Tests Available at the Washington State Department of Health Public Health Laboratories (DOH PHL)

1. Enzyme immunoassay (EIA) for IgM antibody in serum or CSF.
2. Microsphere immunoassay (MIA) for IgM antibody in serum or CSF. This assay is more rapid and specific than the MAC-EIA.
3. PCR assay for viral nucleic acid in blood or CSF (Because PCR is not recommended for routine diagnosis of WNV disease, PCR is not routinely run at the DOH PHL. Consult with DOH CDES if this test is requested, e.g., for a patient with immune dysfunction).

   Until the disease is established in Washington State, DOH PHL will send all positive specimens to the CDC for confirmatory testing by plaque reduction neutralization test (PRNT).

C. Criteria for Testing WNV Specimens at DOH PHL*

All specimens need to be approved by DOH CDES prior to submission.

1. Patients with suspected WNV neuroinvasive disease (fever and change in mental status, cerebrospinal fluid [CSF] pleocytosis, or other acute central or peripheral neurologic dysfunction) when there is no other likely diagnosis.
2. Pregnant or breastfeeding women symptomatic with suspected WNV infection and their neonates or breastfeeding infants.
3. Recent blood, tissue, or organ donors or recipients suspected to have WNV infection
4. Persons with commercial laboratory evidence of WNV infection to confirm the diagnosis (until WNV disease is established in Washington State).

   * Testing for persons who do not fit in these four categories (e.g., WNV non-neuroinvasive disease) should be performed at a commercial laboratory.

D. Specimen Collection

1. Submit > 1 cc of CSF and/or serum (separated serum, not whole blood) for EIA/MIA.

a. Serum should ideally be obtained ≥8 days after onset of symptoms. A second serum specimen will be requested if the first is non-reactive or indeterminate and was obtained less than 8 days after onset of symptoms. To confirm the infection, a four-fold rise in antibody titer should be demonstrated between an acute and convalescent serum specimen

b. CSF obtained less than 3 days after onset of symptoms will be accepted, however, if non-reactive, this will not rule out WNV infection, and a serum specimen obtained 8 days after onset will be requested.

2. Specimens should be refrigerated and transported cold. Frozen CSF is acceptable. Avoid repeated freeze-thaw cycles

   Specimens should be submitted with a completed DOH PHL Virus Examinations form (http://www.doh.wa.gov/EHSPHL/PHL/Forms/VirusExams.pdf)

5. ROUTINE CASE INVESTIGATIONS

Interview the case (or parents) or others who may be able to provide pertinent information.

A. Evaluate the Diagnosis

Review the laboratory report, clinical description and epidemiologic factors such as season, known WNV activity in the area. If laboratory testing is positive for IgM and was done at a laboratory other than DOH PHL, facilitate transport of the specimen or another specimen (i.e., serum or CSF) to DOH PHL for further testing if requested by DOH CDES.

B. Identify Potential Sources of Infection

Obtain a complete travel history and history of mosquito bites during the 15 day period prior to symptom onset. Ascertain whether the case received blood products, tissues or organs within 30 days of their WNV infection. If the patient received blood, tissues or organs in the 30 days prior to onset, contact DOH CDES immediately and inform the blood or tissue bank of the potential source.

C. Identify Potentially Exposed Persons

Determine if the patient donated blood, tissues or organs, breastfed, or gave birth during the communicable period. If the patient donated blood, tissues or organs in the 30 days prior to onset, contact DOH CDES immediately and inform the blood or tissue bank of the potential blood contamination. In cases of potential mother-to-infant transmission, notify DOH CDES and monitor the infant for compatible signs and symptoms for 14 days after last possible exposure.

D. Environmental Evaluation

Notify local environmental health program and/or vector control of locally acquired cases. In outbreak settings, an investigation may assist in identifying and controlling factors favoring transmission.

6. CONTROLLING FURTHER SPREAD

A. Infection Control Recommendations

1. Hospitalized patients should be treated with standard precautions.
2. Cases do not require isolation.
3. Infected persons should be advised not to donate blood, tissues or organs.
4. Infected lactating women should discuss breast-feeding with their medical care provider.

B. Case Management

If the patient received blood products, organs or tissues in the 30 days prior to onset, contact DOH CDES immediately and inform the blood or tissue bank of the potential source.

C. Contact Management

No follow up is needed for household and other close contacts since WNV is not transmitted by close contact. In cases of potential mother-to-infant transmission, notify DOH CDES and monitor the infant for compatible signs and symptoms for 14 days after last possible exposure. Additional testing may be requested. If the patient donated blood products, organs or tissues in the 30 days prior to onset, contact DOH CDES immediately and inform the blood or tissue bank of the potential exposure.

D. Management of Other Exposed Persons

People with recent mosquito bites in areas where WNV is circulating should report symptoms of fever, headache, loss of appetite, rash, stiff neck, etc. to their health care provider.

E. Environmental Measures

Environmental measures to reduce WNV transmission may include the elimination of mosquito breeding habitats and the use of chemical (i.e., pesticides) and biological controls. Consult with local environmental health or vector/mosquito control programs to determine appropriate intervention measures.

7. MANAGING SPECIAL SITUATIONS

A. Presumptive Viremic Donor (PVD)

1. Blood collection agencies routinely screen blood products for WNV during months when WNV is active using nucleic acid-amplification tests (NAT).
2. Blood collection agencies report persons whose blood screens positive to the DOH CDES who, in turn, report the person to the LHJ. Local public health professionals should initiate an investigation using the WNV Case Report Form.
3. Persons whose blood donation screens positive for WNV by either a) one reactive NAT with a signal-to-cutoff value ≥ 17 or b) two reactive NATs using two different primers/methods are considered PVDs and no further testing is indicated.

4. If a person's blood donation screens positive for WNV using a less stringent method, the LHJ should assist in obtaining a serum sample drawn 10-14 days after the date of the donation to test for IgM. If IgM is detected, the person is a PVD. If IgM is not detected, the NAT should be considered a false positive and the case should be closed.

   Note: **Clinical Syndrome and Case Classification:** All PVDs should be entered into PHIMS, classified as "Not reportable", and manually reported to DOH CDES unless WNV illness is documented. If WNV illness develops after the PVD is first reported, please revisit PHIMS to reclassify the patient as a case (see Part 3. Case Definition).

8. ROUTINE PREVENTION

A. Immunization Recommendations

Currently there is no human WNV vaccine available.

B. Prevention Recommendations

1. Reduce exposure to mosquitoes.
   - Make sure windows and doors are "bug tight." Repair or replace screens.
   - Stay indoors at dawn and dusk, if possible, when mosquitoes are the most active.
   - Wear a long sleeve shirt, long pants, and a hat when going into mosquito-infested areas, such as wetlands or woods.
   - Use mosquito repellent when necessary. The most effective mosquito repellents contain the EPA approved active ingredients DEET (N, N-diethyl-m-toluamide), Picaridin, oil of lemon eucalyptus, or IR3535. Read and follow instructions on the label. Permethrin is another long-lasting repellent that is intended for application to clothing and gear, but not directly to skin. In general, the more active ingredient (higher concentration) a repellent contains, the longer time it protects against mosquito bites. Do not over use repellents. Take special care when using repellent on children.
   - Additional information regarding the use of mosquito repellents can be found on the CDC website at: http://www.cdc.gov/ncidod/dvbid/westnile/qa/insect_repellent.htm and http://www.cdc.gov/ncidod/dvbid/westnile/RepellentUpdates.htm
2. Reduce the number of mosquitoes in breeding sites outdoors by draining sources of standing water.
   - Empty anything that holds standing water—old tires, buckets, plastic covers, and toys.
   - Change water in your birdbaths, fountains, wading pools and animal troughs at least twice week.
   - Recycle unused containers that may collect water—bottles, cans, and buckets.
   - Make sure roof gutters drain properly and clean clogged gutters in the spring and fall.
   - Fix leaky outdoor faucets and sprinklers.

ACKNOWLEDGEMENTS

This document is a revision of the Washington State Guidelines for Notifiable Condition Reporting and Surveillance published in 2002 which were originally based on the Control of Communicable Diseases Manual (CCDM), 17th Edition; James Chin, Ed. APHA 2000. We would like to acknowledge the Oregon Department of Human Services for developing the format and select content of this document.

UPDATES

March 2008: In Section 1C, the guideline for timeliness of initiating an investigation was removed.
July 2008: In Section 1C, the CDC WNV Enhanced surveillance form was added.
In Section 4A, additional information was added regarding laboratory tests.
In Section 8B, IR3535 was added as an EPA approved effective mosquito repellent.